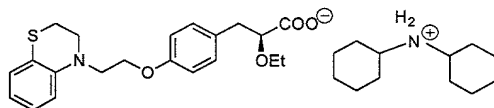


[0052] Mass m/z : 388 ($M^+ + 1$), 130 ($C_4H_{11}N_5$), 113 ($C_4H_8N_4$).

[0053] Anal:Calcd. : $C_{25}H_{36}N_6O_4S$, % C 58.12; % H 6.97%, % N 16.3, Found % C 57.95%, % H 6.61, % N 16.25.

Example 3

Dicyclohexylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0054] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (5.0g) and isopropanol (50 ml) were added to 250 ml four necked round bottom flask fitted with a mechanical stirrer and reflux condenser. The reaction was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. Dicyclohexylamine (2.33g) in isopropanol (20 ml) was added to the reaction mixture at 55-65°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 75-85°C for 12-14 h and monitored the progress of the reaction by TLC. The reaction mixture was concentrated on rotavapor bath at 45-55°C under reduced pressure to its half volume. The concentrated reaction mixture was cooled to RT and stirred for 2-3 h at room temperature. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure dicyclohexylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as off-white crystalline solid (weighs about 5.1 g, yield : 70 %, m.p. : 110°C, purity by HPLC : 98-99 %).

[0055] IR (KBr) cm^{-1} : 2932 (C-H aliphatic stretch), 2700-2200 ($-NH_3$ bands), 1582 ($-COO$ stretch).

[0056] 1H NMR (200 MHz, DMSO- d_6) δ : 1.0 (t, 3H, CH_3-CH_2-O), 1.2-2.0 (m, 22H, Cyclohexyl), 2.4-3.4 (m, 5H, $-S-CH_2$, $Ar-CH_2$, $-CH-Ar$), 3.45-4.0 (m, 7H, $-CH_2-N-CH_2-$, $CHOEt$, CH_2-CH_2-O-), 4.05 (q, 2H, $-OCH_2$), 6.5 (t, 1H, $-CH_2-CH-$), 6.7-7.4 (m, 8H, aromatic).

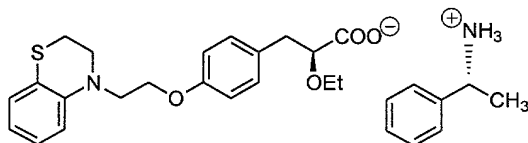
[0057] Mass m/z : 388 ($M^+ + 1$) 182 ($C_{12}H_{23}N$).

[0058] Anal : Calcd. : $C_{33}H_{48}N_2O_4S$, % C 69.71; % H 8.45%, % N 4.92, Found

% C 69.60%, % H 8.35, % N 4.75.

Example 4

(R)-(+)-Methyl benzylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0059] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (5.0 g) and isopropanol (50 ml) were added to 250 ml four necked round bottom flask fitted with a mechanical stirrer and reflux condenser. The reaction was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. R-(+)-Methyl benzylamine (1.5 g) in isopropanol (20 ml) was added to the reaction mixture of 55-65°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 75-85°C for 12-14 h and monitored the progress of the reaction. The reaction mixture was cooled to 25-35°C and stirred for 2-3 h. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure (R)-(+)-methylbenzylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxypropanoic acid as off-white crystalline solid (weighs about 6 g, yield : 91%, m.p. 126-128°C; purity : 98.56 – 99.3 % by HPLC).

[0060] IR (KBr) cm^{-1} : 2983-2856 ($-\text{N}^+\text{H}$ stretch), 1637($-\text{COO}$, Stretch).

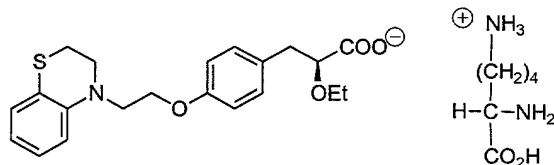
[0061] ^1H NMR (200 MHz, CD_3OD) δ : 1.1 (t, 3H, $\text{CH}_3\text{-CH}_2\text{-O}$), 1.6 (d, 3H, $\text{CH}_3\text{-CH-}$), 2.6-3.4 (m, 5H, $-\text{S-CH}_2\text{-}$; $\text{Ar-CH}_2\text{-}$, $-\text{CH-Ar}$), 3.45-4.0 (m, 7H, $-\text{CH}_2\text{N-CH}_2\text{-}$; $-\text{CH-OEt}$, $\text{CH}_2\text{-CH}_2\text{-O}$), 4.05 (q, 2H, $-\text{O-CH}_2\text{-}$) 6.5 (t, 1H, $\text{CH}_2\text{CH}_2\text{-CH}_2\text{-N-CH}_2\text{-}$), 6.7-7.4 (m, 13H, aromatic).

[0062] Mass m/z : 388 ($\text{M}^+ + 1$), 121($\text{C}_8\text{H}_{11}\text{N}$), 105 (C_8H_8)

[0063] Anal : Calcd. : $\text{C}_{29}\text{H}_{36}\text{N}_2\text{O}_4\text{S}$, % C 68.50; % H 7.08%, % N 5.51, Found % C 68.38, % H 6.9, % N 5.4.

Example 5

L-Lysine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0064] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (2.5 g) and isopropanol (25 ml) were added to the 100 ml four necked round bottom flask, fitted with a mechanical stirrer and reflux condenser. The reaction mixture was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. L-Lysine monohydrate (1.0 g) dissolved in water (5 ml) was added to the reaction mixture at 45-55°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 80-90°C for 20-24 hrs and monitored the progress of the reaction. The isopropanol was distilled off along with azeotropic distillation of water using Dean-Stark apparatus. Fresh isopropanol (25 ml) was added to the residual reaction mixture and cooled the mixture initially to room temperature followed by cooling to 0-5°C under stirring for 60-90 min. The precipitated product was filtered, dried at 60°C for 2-3 hours to afford the pure L-lysine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as off white crystalline, hygroscopic solid (weighs about 2.5 g, yield : 78%, m.p. 142-144°C, purity 97.6 – 99.01% by HPLC).

[0065] IR (KBr) cm^{-1} : 3430-3400 (N-H stretch), 2920 (-C-H aliphatic stretch), 2700 - 2200 ($\text{-N}^+\text{H}_3$ stretch), 1585 (-COO^- stretch), 1400 (-COO^- stretch).

[0066] ^1H NMR spectrum in DMSO-d_6 + TFA (TMS as internal standard) is in confirmation with the assigned structure.

[0067] Mass m/z : 388 ($\text{M}^+ + 1$), 164 ($\text{C}_6\text{H}_{16}\text{N}_2\text{O}_3$), 147 ($\text{C}_6\text{H}_{13}\text{NO}_3$).

[0068] Anal. Calcd for $\text{C}_{27}\text{H}_{41}\text{N}_3\text{O}_7\text{S}$; % C : 58.8; % H 7.44%; % N 7.62%, Found % C 58.7; % H 7.28; % N 7.55.